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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/064,392	07/09/2002	John Hefti	JH-003	5837

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EXAMINER	
SINES, BRIAN J	
ART UNIT	PAPER NUMBER
1743	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/064,392	HEFTI, JOHN	
	Examiner	Art Unit	
	Brian J. Sines	1743	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,8,11,12 and 14-31* is/are pending in the application.

4a) Of the above claim(s) *14-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,8,11 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Newly submitted claims 14 – 31 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1 – 4, 8, 11 and 12, drawn to diffusion-based detection and monitoring methods, classified in class 436, subclass 43.

II. Claims 14 – 31, drawn to a diffusion-based detection apparatus, classified in class 422, subclass 68.1.

The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are related as process of use and product. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the process for using the product as claimed can be practiced with another materially different product. For example, the diffusion-based detection apparatus of invention II, as recited in independent claims 14 and 23, does not positively recite apparatus structure for depositing a reactive constituent in the diffusion channel at a stationary position between the first and second measurement probes.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 14 – 31 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 – 4, 8, 11 and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Yager (U.S. Pat. No. 6,007,775 A).

Regarding claims 1 and 8, Yager anticipates a diffusion based method and device for detecting the activity of a biochemical species in the presence of a reactive constituent within a diffusion channel (20) (see, e.g., col. 1, line 65 – col. 3, line 20; col. 8, lines 8 – 64; figure 1A and 1B). Yager teaches that to measure a detection gradient for an analyte, multiple electrodes can be positioned in series along a diffusion channel (see, e.g., col. 4, lines 48 – 58). Yager teaches that a reagent (150) enters the flow channel through fluid inlet 50 (see col. 8, lines 24 – 31). Yager teaches that a second reagent channel can be positioned downstream of and in series with the first reagent channel for the sequential addition of reagents (see col. 3, lines 7 – 30). Yager teaches that the channel system of the disclosed device and method can be used to

measure concentration of an analyte as a function of distance from the reagent inlet. If the analyte concentration is known, the rate of reaction or activity with the reagent can be obtained from the detection gradient (see col. 11, line 62 – col. 12, line 6). Yager teaches performing kinetic measurements (see, e.g., col. 7, lines 21 – 29). It is inherently anticipated that the disclosed method would employ a correlation step for correlating the measured diffusion gradient response to a predefined baseline diffusion response to determine the reaction rate constant or activity of the biochemical species in the presence of the reactive constituent.

Yager anticipates that the analyte particles diffuse into contact and react with reagent particles. The diffusion detection gradient can be observed at the start 101 and at the end 102 of the detection gradient. The presence of analyte is detected by a change in a property, such as absorbance. The concentration of the analyte can be determined from the distance it takes to change the property, and in particular from the detection gradient (see, e.g., col. 8, lines 32 – 47; figure 1B). Furthermore, Yager teaches that to measure the diffusion detection gradient for an analyte, multiple electrodes or probes can be positioned in series along the channel surface and along the transport axis of the channel (see, e.g., col. 4, lines 48 – 58). Therefore, Yager anticipates obtaining a differential measurement between first and second measurement electrodes or probes, wherein the differential measurement characterizes a diffusion response occurring between the biochemical species and the reactive constituent along the transport axis and between the first and second measurement probes.

Yager anticipates the depositing or introduction of a reactive constituent or reagent at a stationary position between a first measurement probe and a second measurement probe. Yager anticipates that multiple reagent inlets can be positioned downstream and in series along the

channel (e.g., diffusion channel 20) (see, e.g., col. 3, lines 21 – 30; col. 9, lines 27 – 35; col. 10, line 63 – col. 11, line 10).

Regarding claim 2, Yager teaches that the sample concentration of the biochemical species to be detected can be varied (see col. 3, line 62 – col. 4, line 3).

Regarding claims 3, 4, 11 and 12, Yager teaches that the method can use ionic species and cells, and including therapeutic drugs (see col. 4, lines 5 – 22; col. 10, lines 38 – 63).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1 – 4, 8, 11 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yager.

Regarding claims 1 and 8, Yager teaches a diffusion based method and device for detecting the activity of a biochemical species in the presence of a reactive constituent within a diffusion channel (20) (see, e.g., col. 1, line 65 – col. 3, line 20; col. 8, lines 8 – 64; figure 1A).

Yager teaches that to measure a detection gradient for an analyte, multiple electrodes can be positioned in series along a diffusion channel (see, e.g., col. 4, lines 48 – 58). Yager teaches that a reagent (150) enters the flow channel through fluid inlet 50 (see col. 8, lines 24 – 31). Yager teaches that a second reagent channel can be positioned downstream of and in series with the first reagent channel for the sequential addition of reagents (see col. 3, lines 7 – 30). Yager teaches that the channel system of the disclosed device and method can be used to measure concentration of an analyte as a function of distance from the reagent inlet. If the analyte concentration is known, the rate of reaction or activity with the reagent can be obtained from the detection gradient (see col. 11, line 62 – col. 12, line 6). Yager teaches performing kinetic measurements (see, e.g., col. 7, lines 21 – 29).

Yager teaches the depositing or introduction of a reactive constituent or reagent at a stationary position between a first measurement probe and a second measurement probe. Yager teaches that multiple reagent inlets can be positioned downstream and in series along the diffusion channel (see, e.g., col. 3, lines 21 – 30; col. 9, lines 27 – 35; col. 10, line 63 – col. 11, line 10). The applicant is advised that the U.S. Supreme Court recently clarified that a claim can be proved obvious merely by showing that the combination of known elements was obvious to try. In this regard, the U.S. Supreme Court explained that, "[w]hen there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill in the art has a good reason to pursue the known options within his or her technical grasp." An obviousness determination is not the result of a rigid formula disassociated from the consideration of the facts of the case. Indeed, the common sense of those skilled in the art demonstrates why some combinations would have been obvious where

others would not. ("The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results."). See *KSR Int'l v. Teleflex Inc.*, 127 Sup. Ct. 1727, 1742, 82 USPQ2d 1385, 1397 (2007). As discussed above, Yager further teaches the positioning of multiple electrodes or probes along the diffusion channel in series. Therefore, it would have been obvious to a person of ordinary skill in the art to incorporate additional reagent inlets at a fixed stationary position along the diffusion channel, wherein one or more reagent inlets would be positioned between at least two measurement probes to facilitate the detection of a specific reaction product that would act as an indicator that a specific reaction had occurred.

Yager does not specifically teach the use of predefined baseline response data during operation as claimed. However, the use of predefined baseline response data, which would comprise calibration or standard response curves, with detection devices is notoriously well known in the art (see MPEP § 2144.03). Therefore, it would have been obvious to a person of ordinary skill in the art to incorporate the use of predefined baseline diffusion response data with the disclosed method to facilitate effective detection and analysis.

As indicated in figure 1B, Yager teaches that the analyte particles diffuse into contact and react with reagent particles (see col. 8, lines 8 – 61). The diffusion detection gradient can be observed at the start 101 and at the end 102 of the detection gradient. The presence of analyte is detected by a change in a property, such as absorbance. The concentration of the analyte can then be determined from the distance it takes to change the property, and in particular from the detection gradient (see, e.g., col. 8, lines 32 – 47; figure 1B). The concentration data can then be used to determine the activity or rate of reaction of the biochemical species in the presence of the

reactive constituent (see, e.g., col. 11, line 62 – col. 12, line 6). Furthermore, Yager teaches that to measure the diffusion detection gradient for an analyte, multiple electrodes or probes can be positioned in series along the channel surface and along the transport axis of the channel (see, e.g., col. 4, lines 48 – 58). It would have been obvious to a person of ordinary skill in the art to position measurement probes at the start 101 and end 102 locations of the diffusion detection gradient to facilitate concentration measurements for the diffusion detection gradient. Therefore, it would have been obvious to a person of ordinary skill in the art to incorporate the step of obtaining a differential measurement between first and second measurement electrodes or probes, wherein the differential measurement characterizes a diffusion response occurring between the biochemical species and the reactive constituent along the transport axis and between the first and second measurement probes.

Regarding claim 2, Yager teaches that the sample concentration of the biochemical species to be detected can be varied (see col. 3, line 62 – col. 4, line 3).

Regarding claims 3, 4, 11 and 12, Yager teaches that the method can use ionic species and cells, and including therapeutic drugs (see col. 4, lines 5 – 22; col. 10, lines 38 – 63).

Response to Arguments

1. Regarding the rejection of claims 1 – 4, 8, 11 and 12 under 35 U.S.C. 112, second paragraph, applicant's arguments and amendments have been fully considered and are persuasive. This rejection has been withdrawn.

2. Regarding the rejection of the present claims under 35 U.S.C. 102(b) and 103(a) in view of Yager (U.S. Pat. No. 6,007,775 A), applicant's arguments filed 6/28/2007 have been fully considered but they are not persuasive. Yager does specifically teach the depositing or

introduction of a reactive constituent or reagent at a stationary position between a first measurement probe and a second measurement probe. Yager teaches that multiple reagent inlets can be positioned downstream and in series along the diffusion channel (see, e.g., col. 3, lines 21 – 30; col. 9, lines 27 – 35; col. 10, line 63 – col. 11, line 10). As discussed above, Yager further teaches the positioning of multiple electrodes or probes along the diffusion channel in series as well. The applicant is advised that the U.S. Supreme Court recently clarified that a claim can be proved obvious merely by showing that the combination of known elements was obvious to try. In this regard, the U.S. Supreme Court explained that, "[w]hen there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill in the art has a good reason to pursue the known options within his or her technical grasp." An obviousness determination is not the result of a rigid formula disassociated from the consideration of the facts of the case. Indeed, the common sense of those skilled in the art demonstrates why some combinations would have been obvious where others would not. ("The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results."). See *KSR Int'l v. Teleflex Inc.*, 127 Sup. Ct. 1727, 1742, 82 USPQ2d 1385, 1397 (2007). Furthermore, the prior art can be modified or combined to reject claims as *prima facie* obvious as long as there is a reasonable expectation of success (see MPEP § 2143.02). In view of the Yager disclosure, the positioning of the reagent inlets in a fixed stationary position along the length of the diffusion channel depending upon when a certain reagent, such as an indicator reagent, should be introduced into the diffusion channel to detect a certain chemical compound or reaction product would have been predictable and within the skill of a person of ordinary skill in the art. The placement of the probes along the

diffusion channel to monitor for a specific reaction product would have been predictable and therefore within the skill of a person or ordinary skill in the art. Yager also teaches that the disclosed method and apparatus is suitable for multiple analyte detection (see, e.g., col. 2, line 59 – col. 3, line 20). Furthermore, Yager indicates that despite incorporating multiple reagent inlets along the length of the diffusion channel and with the use of sample streams comprising larger particles, stable laminar flow can be expected in the performing of the method (see col. 2, line 36 – col. 5, line 14). Therefore, it would have been obvious to a person of ordinary skill in the art to incorporate additional reagent inlets at a fixed stationary position along the diffusion channel, wherein one or more reagent inlets would be positioned between at least two measurement probes to facilitate the detection of a specific reaction product that would act as an indicator that a specific reaction had occurred. It should be noted that the claimed method simply does not exclude the layered laminar streams of Yager as argued by the applicant. The independent claims do not positively recite that fluid streams containing a biochemical species and a reactive constituent have a distinct boundary or are side-by-side. The applicant's arguments are not commensurate in scope to the claims. ("Many of appellant's arguments fail from the outset because, as the solicitor has pointed out, they are not based on limitations appearing in the claims."). See *In re Self*, 671 F.2d 1344, 1348, 213 USPQ 1, 5 (CCPA 1982).

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian J. Sines, Ph.D., whose telephone number is (571) 272-1263. The examiner can normally be reached on Monday - Friday (11 AM - 8 PM EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill A. Warden can be reached on (571) 272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Brian J. Sines
Primary Examiner
Art Unit 1743